Supplementary Table 1

Measurement	QC Pool Sample Assessment	HILIC neg
		% CV
Process Variability	Biotin – D2	11.43
	Phenylalanine – D8	23.82
	Lauryl carnitine – D3	15.98
Instrument Variability	Tryptophan – D3	1.68
	Inosine – 4N15	0.14

Supplementary Table 2

Pathways	Total	Expect	Hits	Raw p	Impact
Purine metabolism	65	2.18	10	3.28E-05	0.1352
Aminoacyl-tRNA biosynthesis	48	1.61	8	0.000125	0.16667
Glyoxylate and dicarboxylate metabolism	32	1.07	6	0.000494	0.25927
Phenylalanine metabolism	10	0.34	3	0.00362	0.35714
Phenylalanine, tyrosine and tryptophan biosynthesis	4	0.13	2	0.006345	1
Arginine biosynthesis	14	0.47	3	0.009984	0.07614
Alanine, aspartate and glutamate metabolism	28	0.94	4	0.012704	0.08654
Cysteine and methionine metabolism	33	1.11	4	0.022436	0.02184
Citrate cycle (TCA cycle)	20	0.67	3	0.027131	0.1817
Ascorbate and aldarate metabolism	8	0.27	2	0.027162	0
beta-Alanine metabolism	21	0.70	3	0.030917	0.05597
Pyrimidine metabolism	39	1.31	4	0.038904	0.18376
Galactose metabolism	27	0.91	3	0.059078	0.00228
Glycine, serine and threonine metabolism	33	1.11	3	0.095865	0.46284
Histidine metabolism	16	0.54	2	0.098187	0.31147

Supplementary Table 3

Compound ID	Metabolite	Anova (p)	q Value	Max Fold Change	Highest Mean	Lowest Mean
HMDB0000516	Beta-D-Glucose	1.79E-07	1.30E-07	30.751	PO	PT
HMDB0028817	Glutamylglutamine	0.0237401	0.003757	2.146	PO	PT
HMDB0000243	Pyruvic acid	0.0069468	0.001214	2.102	PT	PO
HMDB0000050	Adenosine	3.80E-07	2.44E-07	37.397	PT	PO
HMDB0001138	NAG	0.003444147	0.0006340	70.201	PT	PO
HMDB0000812	NAA	0.032002278	0.0049310	8.1182	PT	PO
HMDB0000912	Succinyladenosine	4.24E-05	1.20E-05	164.489	PT	PO
HMDB0000086	Glycerophosphocholine	7.17E-06	2.82E-06	36.037	PT	PO
HMDB0000211	myo-Inositol	3.85E-09	5.66E-09	5.934	PT	PO
HMDB0000045	AMP	0.0047216	0.00085316	123.323	PT	PO
HMDB0001586	Glucose 1-phosphate	0.0001948	4.58E-05	7.917	PT	PO
HMDB0001178	ADP ribose	3.34E-06	1.54E-06	597.265	PT	PO

Supplementary Table 4

Metabolite	Anova (p)	q Value	Fold Change	Organoids Average ± Std Dev	Tissue Average ± Std Dev
N-Acetylornithine	1.08E-07	8.68E-08	12.40	4086.63 ± 1203.09	329.3492 ± 108.25
Methionine sulfoxide	8.49E-07	4.92E-07	3.43	1986.464 ± 401.70	578.7502 ± 93.50
N-Acetylglutamic acid	0.00344	0.00064	70.20	3877.897 ± 3790. 54	272235.2 ± 445147.2
L-Tryptophan	8.24E-05	2.16E-05	4.81	5408.283 ± 1436 .00	1123.168 ± 843.58
Citrulline	0.117393	0.0169	1.38	4971.899 ± 1475. 61	3584.13 ± 1747.75
N-Acetyl-L-aspartic acid	0.0320	0.00499	8.11	11284.97 ± 2949. 22	91613.69 ± 81300.42
L-Arginine	1.35E-10	3.64E-10	15.63	352814.6 ± 74215.46	22562.2 ± 2749.72
L-Cystine	2.73E-05	8.27E-06	128.41	78577.42 ± 21031.73	611.9112 ± 711.79
L-Serine	2.69E-06	1.3E-06	3.91	31314.52 ± 7230.47	7996.221 ± 1804.73
L-Histidine	1.58E-08	1.89E-08	145.40	64466.53 ± 37166.2	443.3447 ± 139.05
L-Phenylalanine	5.23E-09	7.32E-09	9.07	45068.67 ± 9042.44	4966.138 ± 1014.74
L-Tyrosine	9.65E-07	5.48E-07	3.51	11268.32 ± 2090.98	3207.043 ± 810.46
Glutamylglutamine	0.0237	0.0038	2.14	4609.788 ± 1075.63	2147.602 ± 3808.84